REMARKS

Claim Amendments

Claims 1-33 are currently pending. Claims 14, 23, 32, and 33 have been canceled without prejudice. Claims 1-13, 15-22, and 24-31 have been amended. New claims 34 and 35 have been added. With this amendment, claims 1-13, 15-22, 24-31, 34 and 35 are pending.

Claims 1-13, 15-22, 24, 25, and 27-31 have been amended merely to correct grammatical errors and to correct matters of form. Claim 1 has been further amended to clarify that MAP2K6 refers to mitogen-activated protein kinase kinase 6. Support for the amendment can be found in the specification at, for example, page 2, lines 28-29. Claim 1 has also been amended to provide proper antecedent basis and to clarify that step (b) comprises contacting the assay system "of step (a)" with a "candidate" test agent. Claims 2 and 28 have been further amended to recite that the small molecule has a molecular weight less than 10,000 daltons. Support for the amendment can be found in the specification at, for example, page 15, lines 6-9. Claims 5-7 have been further amended to delete the word "modulator" and substitute the word "molecule". Support for the amendment can be found in the specification at, for example, page 19, lines 15-22. Claim 7 has been further amended to clarify that "PMO" refers to "phosphorothioate morpholino oligomer". Support for the amendment can be found in the specification at, for example, page 20, lines 1-2. Claims 15 and 24 have been further amended merely to correct their dependencies. Claim 17 has been amended to correct matters of form and to delete the phrase "or an agent derived therefrom". Claim 31 has been further amended to recite that the sample is contacted with a probe for "MAP2K6" expression. Support for the amendment can be found in the specification at, for example, page 36, lines 18-23. Claim 31 has been further amended to recite a method for diagnosing "cancer" in a patient, "wherein the cancer is selected from liver, prostate, skin, stomach, and testis cancer", comprising: (a) obtaining a biological sample from the patient, "wherein the biological sample is obtained from the liver, prostate, skin, stomach, or testis"; (b) contacting the sample with a probe for MAP2K6 expression; (c) comparing results from step (b) with a control; and (d) determining whether step (c) indicates a likelihood of "liver, prostate, skin, stomach, or testis cancer". Support for the amendment can be found in the specification at, for example, pages 40-42 and Table 1.

New claim 34 recites "[a] method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of: (a) providing an assay system comprising a

nonhuman animal expressing MAP2K6, wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis; (b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent." Support for new claim 34 can be found in original claims 1, 8, and 14.

New claim 35 recites "[a] method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of: (a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid; (b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent; (d) providing a second assay system comprising a non-human animal expressing MAP2K6, wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis; (e) contacting the second assay system with the candidate test agent of (b) under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and (f) detecting an agent-biased activity of the second assay system, wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the candidate test agent as a candidate branching morphogenesis modulating agent. Support for new claim 35 can be found in original claims 17 and 23.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application.

35 USC §112, Second Paragraph, Rejections

Claims 2, 3, 5, 28, and 31-33 were rejected under 35 USC 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 32 and 33 have been canceled, rendering the rejections moot as to these claims. Applicants specifically address the individual rejections of claims 2, 3, 5, 28 and 31 below.

With respect to claims 2 and 28, the Office alleged that the term "small" is indefinite because it is a relative term that is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonable apprised of the scope of the invention. Applicants submit that the term "small molecule" is not indefinite. First, the term "small molecule" is a term well understood in the art and, second, the specification clearly describes the term "small molecule". Thus, one skilled in the art would be reasonably apprised of the scope of the invention. Despite Applicants disagreement with the merits of the rejection and solely in an effort to advance prosecution, claims 2 and 28 have been amended to recite that the small molecule has a molecular weight less than 10,000 daltons, thus rendering the rejection moot. Support for the amendments can be found in the specification at, for example, page 15, lines 6-9. Applicants respectfully request withdrawal of the 35 USC §112, second paragraph, rejection of claims 2 and 28.

With respect to claim 31, the Office alleged that the recitation of the term "MBM" is vague and indefinite because the term has no literal support in the specification. Applicants submit that the provisions of 35 USC §112, second paragraph, do not require literal or verbatim support in the specification to render the claim clear and definite. However, solely in an effort to advance prosecution, claim 31 has been amended to recite that the sample is contacted with a probe for "MAP2K6" expression (which term is defined in claim 1 and the specification as "mitogen-activated protein kinase kinase 6"). Support for the amendment can be found in the specification at, for example, page 36, lines 18-23. Applicants respectfully request withdrawal of the 35 USC §112, second paragraph, rejection of claim 31.

With respect to claim 33, the Office alleged that the reliance on Table I and the recitation of "having a >25% expression level" without stating to what the expression level is being compared renders the claim vague and indefinite. Claim 33 has been canceled without prejudice, thus rendering the rejection moot. Applicants respectfully request withdrawal of the 35 USC §112, second paragraph, rejection of claim 33.

With respect to claims 5 and 28, the Office alleged that the claims are indefinite in the recitation of the term "nucleic acid modulator". Applicants submit that the specification clearly describes "nucleic acid modulators" as MAP2K6-modulating agents comprising nucleic acid molecules. Accordingly, the claims are clear and definite. However, solely in an effort to advance prosecution, claims 5 and 28 have been amended to recite the term "nucleic acid molecule". Support for the amendment can be found in the specification at, for example, page 19, lines 15-22. Applicants respectfully request withdrawal of the 35 USC §112, second paragraph, rejection of claims 5 and 28.

35 USC §112, First Paragraph, Rejections

Claims 17-25 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Office objected to the recitation of the phrase "an agent derived therefrom" in claim 17, alleging that the specification provides no guidance as to how an agent is actually derived from the test agent of claim 1. Without acceding to the merits of the rejection, Applicants have deleted this phrase from claim 17, thus obviating the rejection. Applicants respectfully request withdrawal of the 35 USC §112, first paragraph, rejections.

35 USC §102 Rejections

Claims 1, 5, and 31-33 were rejected under 35 USC §102(b) as being allegedly anticipated by Wong et al (Gynecologic Oncology, 2001, 82:305-311). Claims 32 and 33 have been canceled, rendering the rejection moot as to these claims. Applicants respectfully traverse the rejections of claims 1, 5, and 31 for the reasons set forth below.

Under 35 U.S.C. § 102(b), a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); M.P.E.P § 2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. § 2131. Furthermore, the prior art reference must provide an enabling disclosure. M.P.E.P. §2121.01; *In re Hoeksema*, 399 F.2d 269 (CCPA 1968) ("In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention' 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'… .").

To anticipate claims 1 and 5, the Wong et al reference must teach a method of identifying a candidate branching morphogenesis modulating agent comprising the steps of: (a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid; (b) contacting the assay system with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.

The Wong et al reference fails to anticipate the present claims 1 and 5 because it fails to teach each and every element as set forth in the claims. The Wong et al. reference merely describes the level of MEK6 expression in normal ovarian cells versus ovarian cancer cell lines and immortalized ovarian tumor cell lines. In contrast to the present invention, the Wong et al. reference does not teach contacting any of the ovarian cells with a candidate test agent and detecting a difference in MAP2K6 between reference cells (i.e., no test agent) and cells contacted with the test agent. Applicants request the Office to point out where Wong et al. teaches administering a test agent to cells and detecting a test agent-biased activity of MAP2K6 polypeptide or nucleic acid. In the absence of teaching step (b) of the claimed method, Wong et al. fails to teach each and every step of the claimed invention and thus fails to anticipate claims 1 and 5.

To anticipate amended claim 31, the Wong et al. reference must teach a method for diagnosing liver, prostate, skin, stomach, or testis cancer in a patient comprising: (a)

obtaining a biological sample from the liver, prostate, skin, stomach, or testis; (b) contacting the sample with a probe for MAP2K6 expression; (c) comparing results from step (b) with a control; and (d) determining whether step (c) indicates a likelihood of liver, prostate, skin, stomach, or testis cancer.

Wong et al. merely teaches determining the level of MEK6 in ovarian cancer cells lines and normal ovarian cells in culture. Thus, Wong et al. fails to teach or suggest a method for diagnosing liver, prostate, skin, stomach, or testis cancer in a patient comprising, among other things, obtaining a biological sample from the liver, prostate, skin, stomach, or testis of a patient. Given that Wong et al fails to teach each and every element of the claimed method, it fails to anticipate claim 31.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §102(b) rejections in view of Wong et al.

Claims 1-6, 17, 19, and 26-30 were rejected under 35 USC §102(b) as being allegedly anticipated by Stein et al (WO97/22704). Applicants respectfully traverse the rejections for the reasons set forth below.

To anticipate claim 1 and claims dependent thereon, the Stein et al reference must teach a method of identifying a candidate branching morphogenesis modulating agent comprising the steps of: (a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid; (b) contacting the assay system with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.

The Stein et al reference fails to anticipate the present claims because it fails to teach each and every element as set forth in the claims. The Stein et al. reference is directed to compositions and methods for potentiating the activity of p38 using MEK6 (MAP2K6). Stein et al teaches contacting a candidate agent with a MEK6 polypeptide and subsequently measuring the ability of the MEK6 polypeptide to activate p38. In contrast to the present invention, the Stein et al. reference fails to even contemplate a method for identifying a candidate branching morphogenesis modulating agent using an

assay system comprising MAP2K6 polypeptide or nucleic acid, much less teach or suggest such method.

Although the Office does not explicitly discuss the preamble of the present claims in the context of the teachings of Stein et al., Applicants presume that the statements made with respect to the Wong et al. reference also apply to the Stein et al reference. Specifically, the Office stated that "the recitation of a method of 'identifying a candidate branching morphogenesis modulating agent' …has not been given any weight because said recitations occur in the preamble." (Office Action at page 5) Citing *In re Hirao* (CCPA 1976) and *Kropa v. Robie* (CCPA 1951), the Office further stated that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process and where the body of the claim does not depend on the preamble for completeness, but instead the process steps are able to stand alone. (Id.) The Office further noted that "the phrase 'wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent' [is] not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited". (Id.)

Contrary to the Office's assertions, more recent case law holds that the determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts of each case. *Catalina Mktg. Int'l v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed Cir 2002). Thus, there is no litmus test defining when a preamble limits the scope of the claim. *Id.* Rather, "a claim preamble has the import that the claim as a whole suggests for it." *Bell Communications Research, Inc. v. Vitalink Communications Corp*, 55 F.3d 615, 620 (Fed Cir 1995). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is 'necessary to give life, meaning and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." *Pitney Bowes, Inc. v. Hewlett-Packard Co,* 182 F.3d 1298 (Fed Cir 1999). Furthermore, clear reliance on the preamble during prosecution transforms the preamble into a claim limitation because such reliance indicates the use of the preamble to define in part the claimed invention. *Catalina Mktg. Int'l v. Coolsavings.com, Inc.* (Fed Cir 2002).

In the present case, it is clear from the title of the application ("MAP2K6 as Modifier of Branching Morphogenesis and Methods of Use") and the content of the entire specification that the recitation of a method of "identifying a candidate branching morphogenesis modulating agent" is necessary to breathe "life, meaning and vitality" into the claim and can not simply be dismissed by the Office as not having any patentable weight. Indeed, the crux of the invention is the discovery of the link between MAP2K6 and branching morphogensis modulation. Thus, the preamble in this case is not merely a statement of effect that may or may not be desired or appreciated, but rather is a statement of the intentional purpose for which the method must be performed. See *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333-34 (Fed Cir 2003).

Furthermore, the determination of whether a "wherein" clause is a limitation in a claim depends on the specific facts of the case. MPEP 2111.04. When a "wherein" clause states a condition that is material to patentability, it can not be ignored in order to change the substance of the invention. *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed Cir 2005). In this case, the phrase "wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent" does not simply express the intended result of a process step, but rather recites a condition that is material to patentability. Thus, when read in the context of the entire claim, including the "wherein" clause, it is clear that the preamble recites limitations of the claim and should be construed as if in the balance of the claim.

Under this claim construction, the Stein et al reference fails to anticipate claim 1 and claims dependent thereon because it fails to teach or suggest a method for identifying a candidate branching morphogenesis modulating agent using an assay system comprising MAP2K6 polypeptide or nucleic acid.

With respect to claim 17, which method additionally recites providing a second assay system comprising cultured cells or a non-human animal expressing MAP2K6 that detects an agent-biased change in an activity associated with branching morphogenesis, Applicants submit that Stein et al fails to anticipate the claim and claims dependent thereon because it fails to teach or suggest a method for identifying a candidate branching morphogenesis modulating agent using a first assay system comprising MAP2K6

polypeptide or nucleic acid and a second assay system comprising cultured cells or a non-human animal expressing MAP2K6 that detects an agent-biased change in an activity associated with branching morphogenesis.

With respect to claim 26, Applicants submit that Stein et al fails to anticipate the claim and claims dependent thereon because, in the absence of any teaching whatsoever of branching morphogenesis modulation, it fails to teach or suggest a method of modulating branching morphogenesis in a cell by contacting the cell with an agent that specifically binds a MAP2K6 polypeptide or nucleic acid.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §102(b) rejections in view of Stein et al.

35 USC §103 Rejections

Claims 1-6, 17, 19, and 20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704). Applicants respectfully traverse the rejections for the reasons set forth below.

The Office Action failed to provide explicit reasoning as to why Stein et al allegedly renders the claimed invention obvious. Applicants submit that Stein et al provides no teaching whatsoever of branching morphogenesis or the modulation thereof. Thus, Stein fails to teach or suggest a link between MAP2K6 and branching morphogenesis modulation and also fails to teach or suggest a connection between p38 and branching morphogenesis modulation. In the absence of any teaching whatsoever of a connection between MAP2K6 or p38 and branching morphogenesis modulation, one skilled in the art simply would not have been motivated to pursue a method of identifying a candidate branching morphogenesis modulating agent using an assay system comprising a MAP2K6 polypeptide or nucleic acid, much less have a reasonable expectation of successfully applying such method.

Likewise, with respect to claim 17, in the absence of any teaching whatsoever of a connection between MAP2K6 or p38 and branching morphogenesis modulation, one skilled in the art would not have been motivated to pursue a method for identifying a candidate branching morphogenesis modulating agent using a first assay system comprising MAP2K6 polypeptide or nucleic acid and a second assay system comprising

cultured cells or a non-human animal expressing MAP2K6 that detects an agent-biased change in an activity associated with branching morphogenesis, much less have a reasonable expectation of successfully applying such method.

With respect to claim 20, the Office admitted that Stein et al do not teach using an assay that measures cell proliferation or cell cycling; however, it alleged that it would have been obvious to use an assay that measures alterations in cell proliferation or cell cycling based on the teachings in Stein et al relating to the diseases associated with the p38 cascade. However, the only assay taught by Stein et al for use in identifying candidate modulating agents is a kinase assay to measure the activity of MEK6 and subsequently the activity of p38. Stein et al. only briefly mention disease conditions associated with p38 in the completely unrelated context of using modulating agents for therapeutic purposes. Stein et al make no mention of p38 associated diseases in the context of assays used for identifying MEK6 or p38 modulating agents and therefore provide no motivation whatsoever to use an assay that would measure alterations in cell proliferation or cell cycling in a method for identifying candidate modulating agents.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al.

Claims 1-6, 8-11, and 17-20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Sodhi et al (Cancer Research, 2000, 60:4873-4880). Applicants respectfully traverse the rejections for the reasons set forth below.

The Office indicated that Stein et al renders claims 1-6 and 17 obvious for reasons previously stated. With respect to claims 8-11 and 18-20, the Office admitted that Stein et al do not teach or suggest an assay that detects an event which is a response to hypoxic conditions or angiogenesis. However, the Office asserted that one skilled in the art would have been motivated to use such as assay based on the teachings of Sodhi et al which allegedly link the activation of MEK6 and p38 to the activation of HIF-1 and subsequent angiogenesis.

Applicants submit that Stein et al do not teach or suggest a method of identifying a candidate branching morphogenesis modulating agent using an assay system

comprising a MAP2K6 polypeptide or nucleic acid (claim 1) or a method for identifying a candidate branching morphogenesis modulating agent using a first assay system comprising MAP2K6 polypeptide or nucleic acid and a second assay system comprising cultured cells or a non-human animal expressing MAP2K6 that detects an agent-biased change in an activity associated with branching morphogenesis (claim 17) for the reasons set forth above. The teachings of Sodhi et al fail to cure the deficiencies of Stein et al. Sodhi et al makes no mention whatsoever of branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

With respect to claims 8-11 which recite a method of identifying a candidate branching morphogenesis modulating agent using an assay system comprising a MAP2K6 polypeptide or nucleic acid in cultured cells or a non-human animal, wherein the assay system detects an agent-biased change in branching morphogenesis, Applicants submit that in the absence of any teaching whatsoever of a link between MAP2K6 or p38 and branching morphogenesis modulation, one skilled in the art would not have been motivated to pursue the claimed methods. Neither Stein et al nor Sodhi et al mention branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and thus the combined teachings fail to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Sodhi et al.

Claims 1-6, 8, 9, 11, 17, 19, and 20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Terada et al (Kidney International, 1999, 56:1258-1261). Applicants respectfully traverse the rejections for the reasons set forth below.

The Office indicated that Stein et al renders the claims obvious for reasons previously stated. The Office admitted that Stein et al do not teach or suggest an assay that measures cell cycling. However, the Office asserted that one skilled in the art would

have been motivated to use such as assay based on the teachings of Terada et al, which allegedly teach that TGF-B activates the TAK-1-MKK6-p38 pathway and results in the transcriptional down-regulation of cyclin D1.

Applicants submit that Stein et al do not teach or suggest the claimed methods for the reasons set forth previously. The teachings of Terada et al fail to cure the deficiencies of Stein et al. Terada et al make no mention whatsoever of branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Terada et al.

Claims 1-6, 8-13, and 17-22 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Matsumoto et al (J. Cell Biol, 2002, 156:149-160). Applicants respectfully traverse the rejections for the reasons set forth below.

The Office indicated that Stein et al renders the claims obvious for reasons previously stated. The Office admitted that Stein et al do not teach or suggest an assay that would measures tubulogenesis and/or apoptosis. However, the Office asserted that one skilled in the art would have been motivated to use such as assay based on the teachings of Matsumoto et al, which allegedly teach a link between the activation of p38 and the negative regulation of the tubulogenic response to FGF-2 and the induction of VEGF-mediated tubulogenesis without activation of p38.

Applicants submit that Stein et al do not teach or suggest the claimed methods for the reasons set forth previously. The teachings of Matsumoto et al fail to cure the deficiencies of Stein et al. Matsumoto et al make no mention whatsoever of branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Matsumoto et al.

Claims 1-7 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) (in view of Iversen).

The Office did not indicate thecite for Iversen. The document listing the references cited by the Examiner does not include the Iversen reference. Applicants will respond to the rejection upon notice of the Iversen reference.

Allowable Subject Matter

The Office stated that claims 14-16 and 23-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have included new claim 34, which covers the subject matter of original claim 14 and new claim 35, which covers the subject matter of original claim 23. Applicant respectfully requests allowance of new claims 34 and 35 and claims 15, 16, 24, and 25.

Conclusion

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If the Examiner has any questions regarding this response, she is invited to call the undersigned attorney.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

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By: /Christopher P. Singer/
Christopher P. Singer, Ph.D.
Registration No. 48,701